

In the Sequence Listing

Please insert pages 1-67 containing the Sequence Listing.

In the Specification

Please amend the specification to read as follows:

On page 4, please delete the paragraph beginning with "The allatostatins" and insert therefor:

-- The allatostatins are an important group of insect neurohormones controlling diverse functions including the synthesis of juvenile hormones known to play a central role in metamorphosis and reproduction in various insect species. The very first *Drosophila* allatostatin, Ser-Arg-Pro-Tyr-Ser-Phe-Gly-Leu-NH₂ <SEQ ID NO:161> (i.e., drostatin-3), was isolated from *Drosophila* head extracts (Birgulet al., The EMBO J., 1999, 18, 5892-5900). Recently, a *Drosophila* allatostatin preprohormone gene has been cloned which encodes four *Drosophila* allatostatins: Val-Glu-Arg-Tyr-Ala-Phe-Gly-Leu-NH₂ <SEQ ID NO:164> (drostatin-1), Leu-Pro-Val-Tyr-Asn-Phe-Gly-Leu-NH₂ <SEQ ID NO:165> (drostatin-2), Ser-Arg-Pro-Tyr-Ser-Phe-Gly-Leu-NH₂ <SEQ ID NO:161> (drostatin-3) and Thr-Thr-Arg-Pro-Gln-Pro-Phe-Asn-Phe-Gly-Leu-NH₂ <SEQ ID NO:166> (drostatin-4) (Lenz et al., Biochem. Biophys. Res. Comm. 2000, 273, 1126-1131). The first *Drosophila* allatostatin receptor was cloned by Birgul et al. and shown to be functionally activated by drostatin-3 via Gi/Go pathways (Birgul et al., EMBO J. 1999, 18, 5892-5900). A second putative *Drosophila* allatostatin receptor (i.e., DARII). has been recently cloned (Lenz et al., Biochem. Biophys. Res. Comm. 2000, 273, 571-577). The DARII receptor cDNA (accession No. AF253526) codes for a protein that is strongly related to the first *Drosophila* allatostatin receptor. However, to date no functional activation of DARII by allatostatins has been reported. --

On page 4, please delete the paragraph beginning with "The sulfakinins" and insert therefor:

-- The sulfakinins are a family of insect Tyr-sulfated neuropeptides. They show sequence and functional (myotropic effects, stimulation of digestive enzyme release) similarity to the vertebrate peptides gastrin and cholecystokinin. A gene encoding two sulfakinins (also called drosulfakinins), DSKI [Phe-Asp-Asp-Tyr(SO₃H)-Gly-His-Met-Arg-Phe-amide] <SEQ ID NO:155> and DSKII [Gly-Gly-Asp-Asp-Gln-Phe-Asp-Asp-Tyr(SO₃H)-Gly-His-Met-Arg-Phe-amide] <SEQ ID NO:160>, has been identified in *Drosophila melanogaster* (Nichols, (Mol. Cell Neuroscience, 1992, 3, 342-347; Nichols et al., J. Biol. Chem. 1988, 263, 12167-12170). The C-terminal heptapeptide sequence, Asp-Tyr(SO₃H)-Gly-His-Met-Arg-Phe-amide <SEQ ID NO: 162>, is identical in all sulfakinin identified so far from insects that are widely separated in evolutionary terms. The conservation of the heptapeptide sequence, including the presence of the sulfated Tyr residue, in widely divergent insect taxa presumably reflects functional significance of this myotropic "active core" (Nachman & Holman, in *Insect Neuropeptides; chemistry, biology and action*, Menn, Kelly & Massler, Eds., 1991, pp. 194-214, American Chemical Society, Washington, D.C.). To our knowledge, to date no receptors for insect sulfakinins have been identified. --

On page 42, please delete the paragraph beginning with "The modulators" and insert therefor:

-- The modulators of the invention exhibit a variety of chemical structures, which can be generally grouped into non-peptide mimetics of natural GPCR receptor ligands, peptide and non-peptide allosteric effectors of GPCR receptors, and peptides that may function as activators or inhibitors (competitive, uncompetitive and non-competitive) (e.g., antibody products) of GPCR receptors. The invention does not restrict the sources for suitable modulators, which may be obtained from natural sources such as plant, animal or mineral extracts, or non-natural sources such as small molecule libraries, including the products of

combinatorial chemical approaches to library construction, and peptide libraries. Examples of peptide modulators of GPCR receptors exhibit the following primary structures:

GLGPRPLRFamide <SEQ ID NO: 49> , GNSFLRFamide <SEQ ID NO: 168> ,
GGPQGPLRFamide <SEQ ID NO: 102> , GPSGPLRFamide <SEQ ID NO: 103> ,
PDVDHVFLRFamide <SEQ ID NO: 150> , and pyro-EDVDHVFLRFamide <SEQ ID NO:
167>. --

On page 95, please delete the paragraph beginning with "Aliquots (5-10 μ l containing 1-5 μ g protein) of cytosol" and insert therefor:

-- Aliquots (5-10 μ l containing 1-5 μ g protein) of cytosol are mixed with 1 mM MAPK Substrate Peptide (APRTPGGRR <SEQ ID NO: 163> , Upstate Biotechnology, Inc., N.Y.) and 50 μ M [γ - 32 P]ATP (NEN, 3000 Ci/mmol), diluted to a final specific activity of ~2000 cpm/pmol, in a total volume of 25 μ l. The samples are incubated for 5 minutes at 30°C, and reactions are stopped by spotting 20 μ l on 2 cm² squares of Whatman P81 phosphocellulose paper. The filter squares are washed in 4 changes of 1% H₃PO₄, and the squares are subjected to liquid scintillation spectroscopy to quantitate bound label. Equivalent cytosolic extracts are incubated without MAPK substrate peptide, and the bound label from these samples are subtracted from the matched samples with the substrate peptide. The cytosolic extract from each well is used as a separate point. Protein concentrations are determined by a dye binding protein assay (Bio-Rad Laboratories). Agonist activation of the receptor is expected to result in up to a five-fold increase in MAPK enzyme activity. This increase is blocked by antagonists. --